Med Trib 13

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and Medical News

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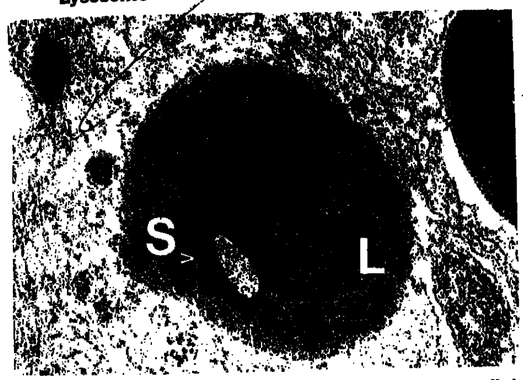
Lysosome 'Tricked' Into Accepting Enzyme



Liposome "spansule" (S) carrying peroxidase and coated with immunoglobulin is shown having fused with dogfish lysosomes (L) within phagocyte in these electron micrographs. Similar method of supplying enzymes to deficient human lysosomes may have application in Tay-Sachs and other degenerative diseases of C.N.S.

Biological Engineering Is Used To Put Enzymes in Lysosomes

By Edward Grossman
Medical Tribune Staff

NEW YORK—Using phagocytes of the dogfish shark, Dr. Gerald Weissmann of the New York University Medical Center and a group of his students have devised a method of "tricking" lysosomes into taking up missing enzymes.

The method, which depends on spansule-like artificial "liposomes" to deliver the enzymes into the lysosomes, may have clinical application in the treatment of a number of sphingolipidoses enzyme-deficiency diseases, including Tay-Sachs Disease, Dr. Weissmann indicated.

Dr. Weissmann told MEDICAL TRIBUNE that preliminary data from in vitro studies of tissue from three Tay-Sachs patients shows "some promise" that the new method could be useful in delivering enzymes efficiently in humans.

The dogfish shark was chosen for an experimental model because it lacks peroxidase, a lysosomal enzyme similar to those which are absent in patients with Tay-Sachs and related disorders. In humans the lack of these enzymes leads to intracellular build-up of unmetabolized lipids in the central nervous system, progressive degeneration, and death.

Dr. Weissmann's group utilized dogfish phagocytes to take up peroxidase enzyme, which had been captured by

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Antiabortion Shift Worries Europe MDs

By James Magee
Medical Tribune World Service

GENEVA—Signs of a conservative political backlash on abortion have left many physicians in Switzerland, West Germany, and Italy wondering whether they are facing prosecution.

In West Germany, legislation that would have brought that country into line with France and the United Kingdom—permitting abortion virtually without restriction during the first trimester—has been blocked by the constitutional court after having been accepted in parliament by a large majority.

Given the scale of abortions in Germany—one estimate puts the total at between 800,000 and 1,200,000 a year—the decision has not only created fresh public controversy but has also caused apprehension and bewilderment among physicians.

In Switzerland, where three projects are under study for a change in the abortion laws, the medical profession is also feeling increasingly exposed.

This has been underlined by the decision by one cantonal court to hand down suspended prison sentences and assess heavy fines against three physicians who have been regularly carrying out abortions.

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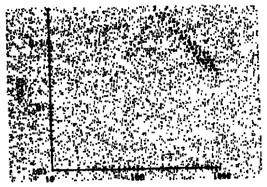
Noninvasive Technique



Average frequency spectrum of 8 systolic bruits in patient with stenosis of residual diameter 2.0 mm. Cross hairs mark "break frequency," at which intensity falls off sharply; frequency was found inversely related to diameter of stenotic segment.

Phonoangiography Indicates Degree Of Carotid Stenosis

By Frances Goodnight
Medical Tribune Staff

HOUSTON—Successful use of noninvasive phonoangiography to predict the degree of carotid artery stenosis in patients with atherosclerotic vascular disease has been achieved by a team of investigators at Massachusetts General Hospital and the Massachusetts Institute of Technology.

A clinical trial of the new technique in 48 patients having carotid bruits yielded results that "compared favorably" with those obtained by a standard carotid arteriogram, the American College of Cardiology was told here.

Describing the procedure, M.I.T graduate student James O. Gruber said that phonoangiography provides quantitative infomation about the relationship between the diameter of a narrowed artery and the frequency-intensity spectrum of the sound produced by turbulent flow at the stenosis.

Data are gathered by placing a pressure-sensitive microphone on the skin over the artery. Bruits are recorded with a tape recorder, the taped signal is transmitted to a minicomputer via an analog-digital converter, and the digitized signal is then displayed on a cathode ray tube.

Dr. Robert S. Lees, one of the research group's senior investigators and director of the M.G.H. Non-Invasive Diagnostic Laboratory, commented during a news conference that he believes phonoangiography will become a useful screening procedure because of its comparative simplicity, its noninvasive nature, and the fact that it can be done on an outpatient basis.

Although Dr. Lees does not expect the new technique to replace arteriography, he foresees that it will serve to

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When to Do T&A? 30 Surveys Fail To Resolve Issue

Medical Tribune World Service

WINNIPEG, MAN.—T&As—should they or shouldn't they be done and when? A team of physicians at McMaster University in Hamilton, Ont., reviewed 30 surveys of tonsilloadenoidectomies, and concluded that all of the surveys were lacking in one respect or another.

If the question is to be resolved, they told the Royal College of Physicians and Surgeons of Canada here, what's needed is—another survey.

The question should be resolved, they said, because T&As are both costly and risky. In Canada in 1971, there were 161,301 of the procedures performed at a cost of $25,600,000 with a mortality rate of approximately one death in 10,000 procedures. Dr. William Feldman who headed the survey team, proposed "a prospective, randomized, controlled clinical trial quantifying outcome by objective tech-

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making rounds — at press time

INTERN & RESIDENT STRIKE in N.Y. City should have "broad range implications for house staff across the country if substantial gains are achieved in the areas of more reasonable hours and elimination of out-of-title work," the president of the Physicians National Housestaff Association, Dr. Robert Harmon, told MT.

TOUGHER LICENSING LAWS are being sought by Washington D.C. Medical Society, according to its president, Dr. William Cooper. "Right now, the law says a physician's license can't be touched unless he's convicted and sentences for a felony. In most other states, medical licenses can be suspended or revoked for professional misconduct," executive director Franc Ferraraccio told MT. The society proposes expanding local licensing commission to include a majority of MDs.

Exclusive Medical Tribune Report—IV

Assessing Adverse Drug Reactions

This is the fourth article in a series presenting highlights from an objective study of adverse drug reactions sponsored by Medicine in the Public Interest. The study was made by two leading pharmacologists, Drs. Fred Karch and Louis Lasagna of the University of Rochester School of Medicine and Dentistry.

The true dimensions of the adverse reaction (ADR) problem was one of the primary interests of the Karch and Lasagna report for Medicine in the Public Interest, a nonprofit organization that carries out research related to health and evaluations "that the government cannot or will not perform" objectively. Witnesses before the Senate subcommittee on health had extrapolated data from a few limited studies to project as many as 140,000 deaths per year from ADRs.

The full MIPI report on adverse drug reactions can be obtained at $1.50 a copy from Medicine in the Public Interest, Suite 720, 600 New Hampshire Ave., N.W., Washington, D.C. 20037.

After reviewing this data, Drs. Karch and Lasagna concluded that these estimates "are completely unreliable" because their data base was "incomplete, unpresentative, uncontrolled and not operationally identified." They pointed out that "no statistically valid estimates can be derived from such data."

Nevertheless they did not dismiss the problem. "One can scarcely think of a more critical issue," they said. "It is one thing if a patient, without a prior history of allergy, develops a severe reaction to an antibiotic, appropriately chosen and prescribed in proper dosage for the proper length of time, in the treatment of lobar pneumonia, and quite another if the same event occurs in someone given the same antibiotic in the same way to treat viral hepatitis. The first represents an unfortunate but necessary risk that must be run, because failure to treat involves worse risks; the second is a totally unjustified risk taken without anticipation of benefit."

Fourth of a Series

Moratorium: "Reckless Statements"

Yet the magnitude of the problem cannot be presently ascertained from available data. This led Drs. Karch and Lasagna to assert "a moratorium on reckless statements and estimates" as well as "more complete data" were "desperately needed."

In the MIPI study Drs. Karch and Lasagna pointed out that one of the deficiencies of many studies was a poor defining of what a drug was, what an adverse drug reaction was, and a general lack of perspective on the problem. "Our survey strongly suggests that alcohol is responsible for more hospitalizations than all the ethical drugs put together," they said in calling for perspective and definitions.

Characterizing a drug as "a chemical substance or product available for an intended diagnostic, prophylactic, or therapeutic purpose for the benefit of the recipient," Drs. Karch and Lasagna defined an adverse drug reaction as "any response to a drug which is noxious and unintended and which occurs at dosages used in man for prophylaxis, diagnosis or therapy, excluding therapeutic failures."

Because one of the major difficulties in "discerning whether a particular event in a given patient is the result of a specific medication or is simply part of the patient's underlying illness," they urged close attention be paid to this complex linkage. They called for establishment of definite standardized assessments, such as "definite," "probable," "possible," "conditional" and "doubtful," as was done by the Registry of Tissue Reactions to Drugs.

"Evaluation of adverse drug reactions based on 'definite' or 'probable' reactions should eliminate many 'false-positive' reactions—that is, reactions which might be interpreted as adverse drug reactions, but in fact are not."

Need for Research

Drs. Larch and Lasagna urged a comprehensive research and educational program that would cover the development of standardized methods of assigning a reaction causally to a specific drug, data on control groups, stratification of the populations because the risk-benefit situation differs with each population, and quantification of the benefits derived from drugs.

They also urged studies of underprescribing drugs. "It is paradoxical that we are said to be an overmedicated society, yet our medicine cabinets are full of untaken drugs. Noncompliance is usually in the direction of failure to take drugs; patients in pain are often undertreated in hospitals; our hypertensive patients are often undertreated . . ." said Drs. Karch and Lasagna.

In calling for federal funding of research in these areas, Drs. Karch and Lasagna pointed out that four years ago an international conference on ADRs was held in Washington. "The conferees agreed on the need for a national approach to drug surveillance. It is unfortunate that we are no closer to a concerted effort to define both the good and the bad effects of drugs, so that their optimal place in our society can be defined," they concluded.

Next week Medical Tribune will present an article by Dr. Dana L. Farnsworth, of the Harvard University School of Public Health and chairman of the Board of Trustees of Medicine in the Public Interest, summarizing current medical opinion with regard to adverse drug reactions following the MIPI report on the problem.

Vitrectomy With New Instrument in Seattle

With its new Vitreous Infusion Suction Cutter, the University of Washington Hospital, Seattle, has become the Pacific Northwest's major referral center for vitrectomies. During the procedure, the surgeon makes a small incision in the eye and, using an operating microscope, introduces the instrument into the opaque vitreous, above. The vitreous is then cut and is removed by suction. A saline solution is simultaneously infused to replace it. Eventually, the saline is supplanted by normal eye fluids.

EEC Expedites Movement of Drug Products

By JAMES MAGEE
Medical Tribune World Service

BRUSSELS—A lot of the red tape that up to now has bedeviled the movement of pharmaceutical products across borders in the European Economic Community has been removed by directives approved here by the E.E.C. council of ministers.

The directives, which come on the heels of the agreement to allow free movement of doctors in the nine E.E.C. member-countries, will help to reduce prices by lowering administrative costs and rationalizing production.

At present the marketing of drugs is subject to special national authorization procedures which vary considerably from one E.E.C. country to another. In addition, a product which crosses a frontier is often again subjected to time-consuming checks to test the drug's degree of toxicity, its therapeutic effects and conformity with its stated formula.

Over the next 18 months, however, member-states must take steps to conform to standard criteria for national authorization, including labeling requirements and quality controls. Once a product has been authorized in one E.E.C. country it will no longer be subject to checks in a second country.

The authorization requirements are searching. A manufacturer who wants clearance must show that he has adequate premises and equipment, the necessary staff to test both the raw materials and finished product, and provide detailed information of the results.

Furthermore, the package leaflet will also have to show all the constituents of the product, the method of preparation, full therapeutic indications, contra-indications and side-effects, dosage, method of administration, and storage advice. The leaflet must also indicate the trademark, distributor's or manufacturer's name and address, and the expiration date if shelf-life is less than three years.

The authorization must be refused, or revoked, if the product proves harmful, does not conform to the stated therapeutic effects, or does not match the manufacturer's declared specifications.

The new rules also include a decision to set up a special E.E.C. committee, consisting of health officials of the nine countries, which will not only supervise the authorization system but also provide a channel for companies who want to seek an authorization valid in several countries at the same time. This will be granted if the product has already been cleared by one E.E.C. country, and the request covers at least five member states.

Pharmaceutical products already in circulation will gradually be brought into the provisions of the new regulations. The rules will not apply, however, to biological products, e.g. vaccines, toxins and serums, human blood products, pharmaceuticals based on radio isotopes, or to homeopathic products.

Hastings Favors Deliberation On Malpractice Legislation

By ALAN FITZGIBBON
Special Tribune Correspondent

WASHINGTON—There are no simple solutions to the medical malpractice insurance crisis and any attempt to enact quick remedial legislation might only compound the problem, one of Congress's leading students of medical liability has warned.

REP. HASTINGS

"All too often before I've seen the Congress quickly try to respond to a crisis, and we don't really come up with the answers," said Rep. James F. Hastings, who has been examining the problem intensively since early last fall and readily concedes that he wants to study it further before proposing any solutions.

Mr. Hastings, an influential Republican member of the House Subcommittee on Health and Environment from New York, sponsored a national conference on medical malpractice here with the American Group Practice Association.

One of the shortcomings the congressman sees in any emergency corrective measures, such as a no-fault bill which Sen. Daniel K. Inouye (D.-Hawaii) introduced in mid-January, is that they deal unequally with the many elements of a complex situation and thus neglect the interests of influential constituencies whose resulting opposition might be strong enough to kill a bill.

Mr. Hastings found two faults with the no-fault approach which he thought unlikely to gain inclusion in any measure that may be passed this year.

First, he said, "I'd have a great concern about saying to the profession of medicine, 'Well, you don't have to be concerned any more as to the quality of medicine since there's automatic coverage.'"

And, he continued, "The contingency fee [which no-fault insurance would negate] is and has been historically within the states' jurisdiction. I don't know of any precedents for the federal government, and certainly the Congress, getting into that kind of issue. There has been a question raised as to the constitutionality of the federal government involving itself in an across-the-board limitation on the contingency fee system.

"So I just think it's going to take a while to come up with reasonable answers to this problem. We can't afford to take the amount of time it would require to fight the American Bar Association and other legal groups on the constitutionality of lawyers' rights to charge contingency fees."

Asked why he thought the malpractice insurance problem had suddenly reached crisis proportions in the last two months, even though coverage rates for both physicians and hospitals had clearly been increasing in recent years, Mr. Hastings responded:

Companies' Moves Cited

"Apparently the insurance companies had never made the moves they made earlier this year in New York State, for example, where coverage itself was actually threatened. I suppose that since this had been primarily a state matter, not enough attention had been paid to it. HEW spent 16 months accumulating information for its report on the problem, but apparently they didn't think it was that serious a problem or if they did, they were taking no steps at all to try to suggest some kind of answers. Nor did I hear from the [medical] profession until this year that this represented a crisis for them."

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Biological Engineering Used in Shark To Introduce Enzyme Into Lysosomes

Continued from page 1

ionization in a phosphate solution within the aqueous spaces of laboratory-manufactured liposome organelles. The enzyme-bearing liposomes were coated with dogfish immunoglobulin so that the phagocytes fused with them as if taking up a virus toward which an immune response had been mounted.

It was found that uptake of enzyme released from these coated "spansules" began immediately within the phagocytes, Dr. Weissmann said, and continued for as much as sixty hours, at a rate exceeding 100 times that of free enzymes and twice that of enzymes introduced in liposomes uncoated with immunoglobulin.

DR. WEISSMANN

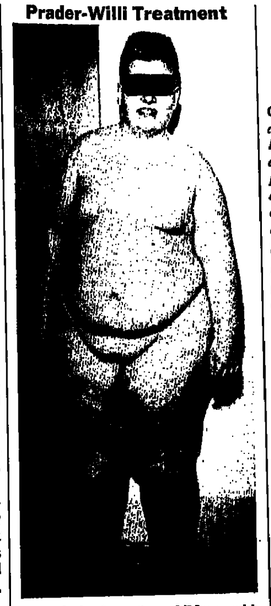
"This is the first successful introduction of enzymes by biological engineering," Dr. Weissmann said. "The method may prove to be of general use in the provision of exogenous enzymes to phagocytic cells genetically deficient in lysosomal hydrolases."

Dr. Weissmann suggested that it might be possible to provide the missing enzyme hexosaminidase A to Tay-Sachs patients by "occasional infusions" of coated liposomes carrying Hex A. Previous attempts at injection of free Hex A as a therapeutic measure have yielded disappointing results.

He cautioned, however, that several problems might have to be overcome in vivo, among them pyrogenicity, and he said that he does not expect clinical trials for a year or more.

The research on dogfish sharks was carried out at the Marine Biological Laboratory, Woods Hole, under a training grant from the National Institutes of Health, while Dr. Weissmann's current work is being supported by the National Foundation-March of Dimes.

Prader-Willi Treatment



A method of treating children with Prader-Willi syndrome, characterized by mental retardation and by compulsive eating, has been developed by scientists at the University of Washington, Seattle. The before-and-after photos, above and below, show the degree of their success in preventing compulsive eating and stimulating mental development. The emphasis is placed on parental motivation and special classroom work. Of the two failures in the program, one was attributed to failure to enlist the mother's cooperation and the other to severe emotional problems due to the death of the father.

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CLINICAL NEWS NOTE: "*. . . all evaluations of the T&A procedure in the English language literature have methodologic defects in study design, sample, description of illness, treatment, and follow-up which preclude the decision on the validity of these procedures.*" *(Dr. William Feldman, see page 1.)*

feature index

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EDITORIAL CAPSULES

. . . brief summaries of editorials or comments in current medical and scientific journals.

New Kind of Leper?

"Persons in medicine, dentistry, and allied professions have an enormous stake in their continued ability to give direct health care. . . . Nonetheless, there is the possibility that an estimated 1 per cent or more of health-care professionals, the carriers of hepatitis B virus (HBV), could be barred from contact with patients. A few are already being treated as if they were a new kind of leper.

"The discovery in 1968 that 'Australia' antigen is a serologic marker of HBV infection provided the ability to identify carriers of that agent. . . .Evidence that contact is sometimes a basis for transmission from person to person has caused Type B hepatitis to be regarded by many as highly contagious. . . . There have been word-of-mouth reports of frightening consequences for health-care personnel discovered through one or another circumstance to have chronic infection. . . . Clearly, a major problem has emerged.

". . . It is necessary to conclude . . . that there is some risk of transmission.

'The Tip of an Iceberg?'

"Do the few incidents in which transmission has been recognized represent very unusual occurrences, or could they be merely the tip of an iceberg? Alter and his associates report that two members of the staff at the Clinical Center, NIH, did not cause 57 patients with whom they had contact in the late incubation period to have risk exceeding that of a control group. Similarly, Williams and his co-workers found that two dentists did not produce hepatitis among 237 patients. . . .

"This information . . . is not necessarily applicable to the risk posed by carriers. It is in this regard that Alter and his colleagues have made their more valuable contribution. The NIH group observed 171 Clinical Center patients for whom three staff members, two physicians and a nurse, provided care. No excess frequency of HBV infection was associated with this carrier contact. As they point out, the proportion of carriers for which their negative result is descriptive is still not known. They have demonstrated, however, that carriers are not necessarily a source of contagion.

"Whatever the cost to individuals, the institutions with which they are associated, or their communities, carriers implicated as a likely source of infection for patients should be excluded from direct care. One should not categorically exclude *all* carriers, however, until there is evidence that this step is actually necessary. . . . It should be recalled that the segregation of lepers was found to be epidemiologically unjustified only after countless lives had been ruined; close and prolonged contact is necessary to transmit leprosy. Let us be certain we do not make a similar mistake . . ." *(Editorial, James W. Moseley, M.D., New Eng. J.M. 292:477, Feb. 27, 1975)*

Abortions Not Up In Asthmatics on Corticosteroids

Medical Tribune Report

SAN DIEGO, CALIF.—The rate of spontaneous abortions in pregnant asthmatics treated with corticosteroids appears to be no higher than what would be expected in the general population, according to a team of researchers from the Northwestern University School of Medicine. Earlier studies indicated that corticosteroids do cause an increased incidence of abortions in animals.

Of 70 pregnancies observed in 55 asthmatics receiving corticosteroid therapy, only one terminated in spontaneous abortion, Dr. Michael Schatz told the 31st Annual Meeting of the American Academy of Allergy here. In addition, there were no maternal, neonatal, or fetal deaths and no increased incidence of toxemia, uterine hemorrhage, or congenital malformations, the Northwestern study showed.

"Except for a somewhat increased incidence of prematurity in our patients, there is no evidence of significantly more complications of pregnancy or fetal outcome in the present series than one would expect in the general population. The reason for the increased incidence of prematurity in this series is unclear, but inasmuch as it was not associated with persistent fetal abnormalities or loss, it would appear to be less significant," Dr. Schatz said.

Anoxia Seen Greater Hazard

"One pregnancy terminated in spontaneous abortion at ten weeks, an incidence of 1.4 per cent," he said. "The patient was not on steroids at conception and received an average of 8.8 mg. of prednisone per day before the steroids were discontinued sixteen days prior to the abortion. The abortion was apparently preceded by increasing asthma not treated with steroids.

"Based on the information reported here, we consider the risk of maternal and fetal anoxia associated with severe asthma a greater potential hazard than the judicious use of corticosteroids during pregnancy."

The study, which is the largest analysis of asthmatics treated with corticosteroids during gestation yet reported, was based on medical records compiled at Northwestern University, the University of Washington and several other medical centers throughout the country.

Collaborating with Dr. Schatz were Drs. Roy Patterson, Stanley Seltz, John O'Rourke and Howard Melam.

IN CONSULTATION

What's new and important in puberty studies?

Part II

The Consultant

DR. ALLEN W. ROOT

Director, University Service, Professor of Pediatrics, University of South Florida, St. Petersburg, Fla.

What are the important clinical points to observe in evaluating a patient with delayed sexual maturation and what studies are available to help differentiate between constitutional delay in growth and development and hypogonadal states?

Girls who have undergone no adolescent changes by 13 years of age and boys by 14 years should be evaluated for delayed sexual maturation. Delayed sexual maturation may reflect merely a slow rate of adolescent development which is a variation of the normal (constitutional delay in growth and development).

In children with suboptimal nutrition (who are underweight for their height) delay in growth and sexual maturation is common. Disorders of the hypothalamus, pituitary and gonads as well as chronic systemic diseases are associated with delayed sexual development.

When evaluating such a patient the personal and family histories should be thoroughly reviewed with attention to the linear growth and weight gain patterns of the patient and the history of sexual development in siblings, parents, aunts and uncles. Past history of medical illnesses, trauma (particularly to the head), eating habits and patterns of weight gain should be recorded. The family history may reveal relatives with similar patterns of delayed growth and development.

Linear Growth Patterns

The child with constitutional delay will have a normal linear growth velocity in a height channel between the third and tenth percentiles or slightly below the third percentile but maintaining a position parallel to the norm. In children with serious organic diseases (deficiency of pituitary function, hypothyroidism, chronic diseases of the cardiovascular, respiratory, urinary and gastrointestinal systems) the linear growth pattern will often reveal progressive deviation away from the normal channel.

In girls the earliest sign of puberty is an increase in the linear growth velocity. Physical examination is extremely important and should include: recording of height, weight, span, lower limb length and blood pressure, evaluation of the general physical status, a search for systemic abnormalities and determination of the stage of sexual maturation. Thorough neurological funduscopic and visual field examinations should be performed.

The earliest sign of puberty in the boy is testicular enlargement, while in girls breast budding is most frequently the first physical sign of adolescence. In younger boys very small testes may suggest a primary testicular abnormality (Klinefelter's syndrome) while in older males gynecomastia and a eunuchoid body habitus are also present. Some subjects with Klinefelter's syndrome may be significantly virilized. In patients with gonadotropin and growth hormone deficiencies the testes may also be small. In girls with delayed adolescence stigmata of gonadal dysgenesis (Turner's syndrome) should be sought: short stature, webbed neck, characteristic facies, shield chest, hypoplastic nipples, increased carrying angles, increased numbers of nevi and history of edema of the dorsom of the hands and feet.

If the historical review and physical examination do not provide specific diagnostic leads the following studies are undertaken:

1) bone age determination: in patients with constitutional delay in growth and development, height and bone ages are usually equally retarded behind, but more than 75 per cent of, chronologic age;

2) skull x-ray will provide information concerning the size of the sella turcica, perisellar calcification and intracranial pressure;

3) buccal smear examination should be done in all girls with delayed adolescence and if there is any clinical suspicion of gonadal dysgenesis chromosome karyotyping should be performed. Occasionally laparoscopy and direct visualization and biopsy of the ovaries may be required;

4) measurement of serum LH and FSH concentrations is of aid in identifying the subject with hypergonadotropic hypogonadism but may not distinguish between patients with hypogonadotropic hypogonadism and constitutional delay in development;

5) the LH secretory response to Gn-RH will identify the latter subject who will have a prepubertal but definite increase in LH levels following Gn-RH administration, while the subject with hypogonadotropic hypogonadism will often have undetectable levels of LH before and after stimulation. Prolonged administration of Gn-RH eventually stimulates LH secretion in many subjects with hypogonadotropic hypogonadism indicating that in most instances this abnormality resides primarily within the hypothalamus;

6) measurement of plasma levels of testosterone or estradiol document gonadal function. Direct estimation of testicular responsivity may be performed by measuring plasma testosterone concentrations before and after administration of human chorionic gonadotrophin (hCG) (2000 units i.m. for three days);

7) ancillary studies of endocrine function (assessment of growth hormone, thyrotropin secretion), and of other systems should be performed as indicated.

What are the recommended approaches to therapy in these conditions, and the best time to start?

In patients with primary hypogonadism (abnormalities of the testes or ovaries) therapy should be started at the usual age of puberty. In boys with Klinefelter's syndrome, anorchia or other forms of testicular dysfunction, treatment with testosterone (testosterone enanthate 50-100 mg. intramuscularly monthly or methyltestosterone 10-20 mg. orally daily) should be initiated at 13 years of age or as soon thereafter as the diagnosis is established even if there is evidence of endogenous androgen secretion in order to ensure more adequate physical and psychosexual maturation and to prevent development of the eunuchoid body habitus. In girls with gonadal dysgenesis estrogens may be initiated at 13 years, although some physicians prefer to begin treatment at 15-16 years in order to permit maximal attainment of linear growth prior to estrogen-induced epiphyseal fusion.

In this writer's opinion treatment should not be delayed at the expense of significant emotional trauma to the patient who invariably compares her state of breast and adolescent development with that of her peers. In this instance adolescent sexual development compensates for the sacrifice of several millimeters of height. Ethinyl estradiol (0.05-0.1 mg. orally in cycles of 21 days on, 7 days off) or estradiol benzoate (1-2 mg. intramuscularly monthly) will usually be sufficient to feminize the child. Progesterone may be added to the regimen later if breast development is insufficient or if menstrual flow is "ragged". The use of synthetic androgens has been advocated in order to increase height in children with gonadal dysgenesis. There are no convincing data to indicate this treatment is of benefit.

In adolescents with hypogonadotropic hypogonadism treatment with gonadal sex hormones is indicated to bring about secondary changes of puberty. Some workers may prefer to employ gonadotropins (hCG, human menopausal gonadotropins) in these patients but this writer defers the use of gonadotropins until fertility is desired. The use of Gn-RH in these patients has not been fully evaluated but may prove to be most physiologic method of treatment.

A Treatment Controversy

There is controversy concerning the treatment of the boy with constitutional delay in growth and adolescent maturation. The majority of these boys and their families are helped by assurance that the boys are normal and that puberty will occur, although at a later age than in the average boy. On occasion positive benefit may be anticipated by treating a boy with constitutional delay in sexual maturation if that boy is exceptionally disturbed by his body image relative to that of his peers. In these instances testosterone enanthate or methylestosterone employed *intermittently* with frequent clinical assessment and bone age determinations may be employed.

Care must be taken to be certain that undue acceleration of skeletal maturation does not occur. It must be emphasized that the object of treatment is only to accelerate the rates of linear growth and sexual maturation and that treatment is terminated when there are signs (testicular enlargement) of activity of the patient's hypothalamic-pituitary-gonadal axis, HCG may also be used in such boys.

Some authorities advocate the liberal use of androgens in boys with constitutional delay, but this writer prefers to reserve therapy for those boys with marked delay who are deeply disturbed by their immature physical appearance.

Continued on page 15

Next In Consultation

DR. JAY N. COHN, Professor of Medicine, Head, Cardiovascular Section, University of Minnesota Hospital, Minneapolis, Minn.

. . . will discuss what's new and important in the management of heart failure and the application of long-term vasodilator therapy in chronic congestive heart failure, the use of nitroglycerin in acute myocardial infarction, and the place of norepinephrine, isoproterenol and other beta-adrenergic stimulatoy drugs in cardiogenic shock. He will also discuss the current status of intra-aortic balloon counterpulsation in cardiogenic shock in acute myocardial infarction.

"Let me tell you about the medicine I'm going to prescribe

TALKING OVER VALIUM®(diazepam) THERAPY WITH YOUR ANXIOUS PATIENT.

A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms. And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication—all of which can have an undesirable effect on the management of the patient's condition.

"It's important that you follow my directions closely."

"I'll see you again the week after next and we'll see how you're making out."

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

for individualized treatment of psychic tension

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Please see the following page for a summary of product information.

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

On the Dispensing of Drugs

The best laid schemes o' mice and men gang aft a-gley.—Robert Burns

It would appear that a number of leaders in the pharmaceutical professions are leading their members into a terrible dead-end. As in *The Nutcracker Suite*, they are having visions of sugarplum fairies—dreams of huge profits. These visions may lead their profession to disaster. Through brilliant and persistent lobbying, they may succeed in overturning a range of traditional patterns in the dispensing of drug prescriptions. Profit mark-ups will, in their plans, be displaced by fees; generic prescribing will replace specifications of particular manufacturers' drugs; anti-substitution laws will be repealed.

Major Drug Costs Lie in Distribution

There is a very conscious effort by some pharmacy leaders to bring about a redistribution of the prescription dollar—ostensibly in the interests of "economy"; practically, in the presumed economic interest of the pharmacist. What is overlooked by the proponents of some of these plans is the fact that fifty per cent or more of the prescription cost of a trademarked drug does not relate to its research, its raw materials, its manufacture, its product liability insurance or its promotion or scientific communication—but to its distribution. *In respect to generic prescriptions, up to 80 or 90 per cent or even more may relate not to the cost of the drug but to the cost of its distribution.* The drive for a fee structure may not significantly reduce the prescription price at the pharmacy but will increase the profit of the pharmacist—temporarily.

The Liability For Drug Disaster

To repeal the antisubstitution laws is a dangerous ploy as was tragically demonstrated by the "Russian roulette" involved in regard to potency variations of digitalis glycosides. Pharmacists as well as physicians would do well to recognize that in the present distribution system protection against drug disaster due to drug defects rests in the control sector of the manufacturer and liability falls on his shoulders. Aside from the large, major companies, very few of the small generic manufacturers would have the fiscal viability to survive and meet the costs of a drug disaster which would then fall upon the pharmacist and/or physician.

The inherent illogic of the drive to replace trademarked prescription drugs at the pharmacy by "cheap" generics is implicit in the false suggestion that a generic drug costs patients but a fraction of a trademarked drug. Untrue. If a shift to generics took place on this premise, retail pharmacists would face a financial disaster. That is the reason for the proposals for dispensing fees and that is also the Achilles heel of this plan of short range expediency and long range disaster.

Who Knows Best—Pharmacist or Physician?

The advocates of the dispensing fee say the pharmacists know more about drugs than physicians. Do they? Do they also know more about the patient, or the patient's diseases? They know less about these than the physician does and may know practically nothing about the physician's therapeutic objectives. It does not serve the professional pharmacist to restructure the distribution systems of drugs because such a development will not only reduce progress in the fields of therapeutics, in which he should be and is interested, but, worse for him, it will point a direction that can constitute economic disaster for pharmacy.

Members of our legislatures and of government agencies that are pressing for changes in present economic patterns of drug manufacture focus on presumed economic savings that they wish to achieve as part of their plan for either national health insurance or, ultimately, the nationalization of medicine. The pharmacists would do well to consider, "How long will the pharmacy retain economic independence if third party payments take over and/or if medicine is nationalized?"

Doctors' Dispensing May Save Hundreds of Millions

If economics is the sole issue in respect to drug prices, generic drugs and repeal of the antisubstitution laws, then consider the following: The greatest savings that can be made in respect to the cost of prescription drugs is not in the area of its research, of its control, of its promotion, and its production—the largest single element of cost in respect to a prescription drug is in its distribution. This is true for the trademarked drugs and even more true for the generic drug. It is inevitable that the government budget boys will soon see this and sharpen their pencils.

What will be the role of the pharmacist if the government and third party payers propose in the interest of economy that physicians dispense fifty or one hundred of their most frequent prescriptions—and do so at a dispensing fee of one dollar (not $2.50) over cost? With one stroke this would achieve a savings of hundreds of millions of dollars. Moreover, it would save the patient the time necessary to go to the pharmacy to have the prescription filled. It would speed the therapeutic process and afford closer patient management.

Untested Systems May Be Dangerous

MEDICAL TRIBUNE does not believe it is in the interest of either the patient or the medical or pharmaceutical professions to destroy existing channels of distribution before other systems have either been tested or put into place.

"My God, that's my psychiatrist!"

MEDICAL TRIBUNE believes it is potentially disastrous to gut antisubstitution laws whose repeal will inevitably be followed by dissatisfaction when the hypothetical savings that are promised do not materialize and when preventable drug disasters ensue. MEDICAL TRIBUNE does not believe it wise to distort or destroy the present relationship between the professions of pharmacy and of medicine. MEDICAL TRIBUNE believes it would be disastrous to entice professional pharmacy for short term gains onto a path which can lead to its eventual economic and professional destruction. *No loosening of restrictions on pharmacists can long prevail at the cost of increasing restrictions on the physician.*

When pharmaceutical organizations play a political game pitting pharmacists and pharmaceutical manufacturers against each other and pharmacists against doctors and, ultimately, doctors against both the pharmacists and the manufacturers, they play with fire. They are exposing their constituencies to the dangers of government economy measures in the areas of prescription drugs which at the very least would place increasing economic restrictions on pharmacists, or lead to the return of drug dispensing in the physician's office. Any actions contributing to increasing governmental economic regulation in the health care field will contribute ultimately to a nationalization of health services which will not be restricted to physicians but must inevitably encompass pharmacists as well. A.M.S.

LETTERS TO TRIBUNE

Beck's Bypass Approach

I was personally very much interested in the article, "Bypass Grafts to Coronary Veins", (MT, Mar. 5). During my association with Claude Beck for over thirty years, I recall that he had carried out a saphenous graft bypass from the aorta to the great vein of the base of the heart.

In the 1949-50 period, he had done several dozen on bull dogs. Following this in several separate operations or steps, he would completely ligate each main coronary artery near its origin.

In 1951, I was present when three dogs whose three main coronaries had previously been ligated were exposed and a clamp placed across the bypass. Much to our surprise, their hearts continued to beat. Later they were sacrificed.

After careful examination and perfusion, it was found that the septal branch of the coronary tree had enlarged and become the main source of the arterial blood to a beautifully developed collateral circulation. (Normally the dog has a relatively larger septal branch than the human).

During the period 1950-52 he must have performed this operation (he called it the Beck II) on 12-15 humans. At the same time he introduced an unique aortic clamp. He appeared to give up this phase of trying to improve the collateral circulation of the heart for two main reasons: (1) a number of the bypasses thrombosed; (2) co-incidentally at the same time he temporarily lost his academic appointment.

The authors are to be complimented on their work and their refined approach.

ROBERT M. HOSLER, M.D.
Cleveland, O.

Time-saving Questioned

Your front-page report (MT, Feb. 19) on the Pfizer produced Autobac I states that the new machine will shorten the waiting time for test results by one day as compared with the traditional Kirby-Bauer method.

This seems hardly possible, because in our laboratory the Kirby-Bauer method takes only 6-8 hours from start to the end. A culture available in the morning for testing will be done with by late afternoon. After 6 hrs. of incubation preliminary readings are available and at 8 hrs. the final report may be sent out.

There will be some time-saving with Autobac I, but it will be of only 2-4 hrs. In my general pediatric practice there has been not one instance in 1974 where such earlier availability of test results would have been needed or where it would have made any difference in patient management.

I believe that the investigators are too optimistic if they think that the nation may save up to 100 million dollars with the new $19,000 laboratory machine. The instances where Autobac I will actually shorten the hospital stay will be few and far between.

ALFRED W. BAUER, M.D.
Kirkland, Wash.

30 Surveys Reported to Fail In Telling When to Do T&As

Continued from page 1

niques." Such a study is essential, he said, to answer whether T&As should be done, and if so, when.

In the past, Dr. Feldman said tonsillectomies have been performed for indications ranging from "routine removal" to "pigeon-breast" to "retarded mental development due to anoxemia." While physicians and surgeons have been more selective in recent years, he noted, T&As were being done in the province of Ontario in 1971 at the rate of 174 procedures per 10,000 children.

Dr. Feldman and his associates—Drs. W. Shaikh, E. Vayda, and B. Haynes—devised a point system to evaluate all the evaluation studies of T&A reported in the English literature in the last 50 years. Points were given for categories of study design, sample, accuracy of description of therapy, and precision of follow-up. Those studies that were most objective in these areas were awarded the most points while those studies that were poorly done, poorly documented, and reflected bias were given the fewest.

In the category of study design, for example, the highest score was given to a randomized design and the lowest to a descriptive one. In the "sample" category, the highest score was given to a study in which the patients most closely represented the general population. For the description of illness before therapy, points were given on the basis of how well the symptoms were quantitated and if reproducible criteria were established for the selection of T&A on the basis of these symptoms.

Points were given in the therapy category if the operation was decribed and complications of surgery and anesthesia were noted. Description of follow-up was scored in terms of objectivity. When follow-up consisted of a questionnaire to parents, for example, it was given a low score because, Dr. Feldman said, this form of questionnaire has been shown to be "grossly inadequate." Further points were given for frequency of observation, objective documentation of physican findings, and relevant laboratory findings.

With this scoring system, an ideal study could score 34 points. But of the 29 studies the team assessed, the highest any one scored was 18 points. "Only one study scored more than 50 per cent of the ideal score. The remaining 28 studies scored less than 40 per cent," says Dr. Feldman. "We conclude, therefore, that none of the studies has conclusively proved whether T&A is beneficial or not."

Moses Swick Honored

Dr. Moses L. Swick, discoverer of intravenous urography, was recently given the degree of Honorary Doctor of Medicine by the Free University of Berlin. Dr. Swick spent the years 1927-30 in Germany on a special fellowship from Mount Sinai Hospital, New York, and conducted much of his research there.

Phonoangiography Gauges Carotid Stenosis

Continued from page 1

identify patients who do not need such an examination and thus could cut down on the number of arteriograms performed.

In the Boston study, phonoangiograms were performed on 61 carotid bruits in 48 patients. All patients also underwent carotid arteriography, and artery measurements obtained by both methods were compared.

Bruit amplitude characteristically reached maximum intensity in the higher frequencies and then began a sharp decline, Mr. Gruber reported. The frequency at which this decline started was termed the "break frequency."

To be acceptable for analysis, intensity spectra were required to show a single clear break frequency, and the slope of the decline had to correspond to the theoretical distribution of turbulent flow. Of the 61 tests, 11 did not produce the pattern of a single clear break frequency and hence proved unusable.

An Inverse Relationship

The investigators found that the diameter of the stenotic segment is inversely related to the break frequency, according to the following equation: the smallest diameter of the stenotic segment equals the peak systolic velocity distal to the stenosis divided by the break frequency.

In the 50 acceptable tests, the diameter of the stenotic segment as obtained by phonoangiography was compared with the diameter obtained by standard radiographic arteriography.

Using 500 mm/second as the value for peak systolic velocity, the difference between these two diameters was less than 1 mm in 73 per cent of the study cases with residual lumen of 5 mm or less, with a mean difference of ± 0.69 mm.

But even better correlation was achieved when an empirical relationship was determined between blood flow velocity and the bruit intensity, Mr. Gruber noted, since the flow of blood through the stenosis and the intensity of the bruit both decrease as stenosis becomes more severe.

Standard arteriograms and phonoangiographic studies analyzed with the help of empirically derived (rather than assumed) flow velocity agreed to within 1 mm in 84 per cent of the case studies where the residual lumen was 5 mm or less, with a mean difference of ± 0.52 mm.

"We believe that phonoangiography is of clinical value now for assessment of carotid artery disease," Mr. Gruber said. "Studies are in progress to determine its usefulness in the diagnosis of femoral artery and aortic valve stenosis."

Other members of the joint research team are Drs. G. Duncan and G.S. Myers, and C.F. Dewey, Jr. Ph.D.

Abidjan Parley on Sickle Cell Anemia Finds U.S., African Approaches Vary

Medical Tribune World Service

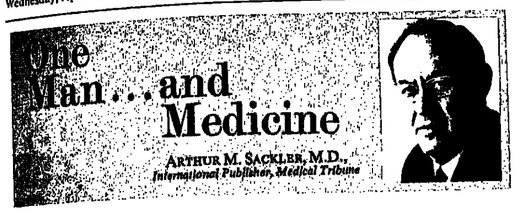
ABIDJAN, IVORY COAST—Physicians attending an international symposium here on sickle cell anemia found there are some substantial variations in approach to the disease between Africa and the United States. These differences are seen both in clinical management of the disease and in genetic counseling aimed at preventing it.

Dr. Charles F. Whitten of Wayne State University told MEDICAL TRIBUNE that Africans "don't accord counseling the same high priority that we in the United States do at the moment, chiefly because they don't have the money for detection and counseling." Also, he said, the sickle cell patient seen in Africa tends to be suffering from multiple health problems, rather than sickle cell disease only.

Dr. Whitten added that he feels the conference, which drew participants from North and South America, Europe, and Africa, "gave us a good opportunity to exchange experiences and to compare where we are."

Another American who attended, Dr. Charles M. Peterson of Rockefeller University, also noted the difference in clinical practice. "About 25 per cent of the sickle cell patients we see are usually suffering from an additional problem," he told MEDICAL TRIBUNE. "But in Africa, you can almost assume that a patient with sickle cell anemia has malaria plus several other infections."

Dr. Paul F. Milner, of the Center for Disease Control, saw yet another difference, one imposed by different systems of health care. "In this country," Dr. Milner told MEDICAL TRIBUNE, "we find most of our sickle cell patients in the big cities. In Africa, a lot of patients are being treated in the urban areas, but I think a large part of the patient population may still be in the rural areas."



Of Time and Life—Part I

"A rose is a rose is a rose."

LIFE'S TANGLED tracks crisscross and overlap. I was in Paris with Peter. Peter was American, a reporter and our French correspondent. As usual we discussed "business" as we went the round of exhibitions. It was after World War II. There was a retrospective of Picasso's paintings at the Museum of Decorative Arts. "This time, Arthur," said Peter, "you can't duck out. I have told Alice Toklas about you so often. She wants to meet you. You'll have to take the time."

Time, as you may have gathered by now, is my greatest enemy. *Time*, not oil, is man's most scarce resource. *Time* is a vicious dictator, inflexible, inexorable—and ultimately always the victor. Because of *time*, its lack, I missed meeting Gertrude Stein. Because of *time*, I missed Picasso (I will tell you about that some other time). "Okay, Peter, to hell with deadlines, let's go."

Of Sound and of Rhythm

Gertrude Stein was a quintessential American spirit. "A rose is a rose is a rose" is no nonsense rhyme. It is the celebration of American English. A rose is more than color, more than smell, more than form. It is the beauty of our language, of sound and of rhythm. I must tell you the story of the Spaniard praising the beautiful sound of English to an American. "Beautiful, like what?" asked the American. "Oh, the beauty of 'sella d'or'," ecstasized the Spaniard.

"What was that?"

"Sella d'or."

"Write it out."

"Oh, you mean 'cellar door'."

Gertrude Stein, the ultimate intellectual, was a classical if not corny American in almost every conceivable way —her rebellious spirit and personal dress, her unorthodox insights and her derogation of sham. This unashamed, self-confessed giant of a mind, who accepted the intellectual and creative talents of very few as genuine (only such as Picasso and Whitehead), loved the song, *The Trail of the Lonesome Pine*. She unabashedly adored the genuineness of the doughboys of the first World War and the GIs of the second. Gertrude Stein loved America, she loved our language. All her writings rejoiced in the beauty of American speech and thought, American adventure and directness. But more about this on another occasion. *Time* is the problem here again.

Back to Gertrude

Oh, yes, what has Gertrude Stein got to do with One Man and Medicine? If there ever was one Lady in Medicine who *really* had an impact on history, it was Gertrude Stein.

When I came into Alice Toklas' apartment, I saw a little old lady surrounded by the "modern" glories of the Gertrude Stein collection in an "ancient" apartment.

"Tell me about 1906 and 1907. There seems to be an acute and sharp break in the Picasso retrospective. A new vision opened with a simple painting which looked to me like a diaper hanging on a line." In those days I was still in the full flush of "febrile" psychoanalytic interpretation. To me that picture signified rebirth.

Exchange of Paintings

Alice Toklas said Picasso was wrestling with new ideas. Her recollections were a bit different than those of Gertrude Stein, as they were in regard to a number of other events. After Picasso and Matisse were introduced to each other, Gertrude Stein said, "They exchanged pictures as was the habit in those days." Each painter chose one of the other's that presumably interested him the most, but these "friends" did not necessarily pick the best one and "used it as an example . . . of the weakness of the other one." This is not the way Alice Toklas remembered the happening. Alice said that after a number of exchanges of paintings, Gertrude said to Picasso, "Pablo, you are a pig. Henri [Matisse] gives you some of his best paintings and you give him your worst." Picasso replied, "He shouldn't be a fool."

I remember at a retrospective of Matisse in the Museum of Modern Art in Paris, I was stunned to discover that the most beautiful Matisse paintings there were almost invariably from Picasso's personal collection. So I concluded that Alice Toklas had the story straight.

Alice Toklas couldn't resist the opportunity to take a poke at the establishment. "You know," she remarked, "when the curators were here to select paintings for Picasso's retrospective, they originally passed up some of Pablo's best Cubist paintings. 'Oh,' they said, 'you have some Braques'." Those Cubist Picasso's are, of course, and always will be some of the most beautiful manifestations of art. They represent the flowering of Spanish genius, growing in the soil of France where it was lovingly tendered by an American physician.

That day we talked quite a bit about Cubism. The fire of debate as to its origin still glowed. Gertrude Stein had claimed that the two closest influences on Picasso in the creation of Cubism were not African art but late Cezanne and actual Spanish landscapes. The Spanish villages which Picasso had recently visited were typical—they cut into and did not follow the landscape. The colors of early Cubism as you will recall were yellows, beiges and faint greens. Stein said that these were typical of the Spanish landscape. For Gertrude Stein, Cubism, real Cubism, was Spanish Cubism, the Cubism of Picasso and Juan Gris.

Influence of African Sculpture

It would be nice if there were always a simple unity of cause. I've had some Picasso drawings and studied some of his sketches for the Demoiselles d' Avignon. There is, for me, particularly in the heads, as well as bodies, not just Spanish landscape but African sculpture as well. Who am I to say whether the influence was direct or indirect, whether it was African sculpture or Spanish architecture and art. I enjoy my opinions* but you may prefer the first-hand reports of Gertrude Stein, the American physician who, as a medical student, had delivered babies of the poor in Baltimore, and later in Paris was midwife at the birth of so much of the then reviled and now admired classics of modern art and aesthetics.

*My feeling may not be so far out. Gertrude Stein, in acknowledging the impact of African statues on the School of Paris, noted that Matisse, who was the first to be influenced in his sculpture, "drew Picasso's attention to it."

EPIGRAMS - Clinical and Otherwise

In medicine, sins of commission are mortal, sins of omission venial.

Theodore Tronchin (1709-81)
Quoted in *Bulletin* of New York Academy of Medicine, V (192)

Cases of Hydatid Disease Rise in Canada and U.S.

Medical Tribune World Service

WINNIPEG, MAN.—Hydatid disease, a parasitic condition most often seen among sheep-raising peoples, is being seen with increasing frequency in Montreal, Dr. Nathan M. Sheiner told the Royal College of Physicians and Surgeons of Canada here.

Twenty hydatid disease patients have been treated at the Montreal Jewish Hospital in the past 11 years, he said, 15 of them in the past five years. He noted that all have been immigrants—11 from Greece, five from the Middle East, and one each from Italy, Spain, Portugal, and Armenia.

In the United States, there has also been an increase in cases, according to reports from the Center for Disease Control in Atlanta. Previously, the C.D.C. said, cases had been confined to a few areas in California and Oregon. The new cases are being seen among Indian sheep-herding tribes in the Southwest. A C.D.C. spokesman said efforts to halt the disease are largely educational.

He recommended that the diagnosis of hydatid cyst be considered in every patient who comes from a geographical area where hydatid disease is endemic, and who presents with abdominal pain, jaundice, hepatomegaly, abdominal mass, or a pulmonary mass lesion.

Medicine on Stamps

Aesculapius

In Greek mythology, Aesculapius was the son of Apollo and Coronis, received his medical education from the centaur Chiron, and was killed by Zeus with a thunderbolt because Pluto complained that through his great medical skill, Hades was being depopulated. In real life, Aesculapius, born about 1300 B.C., was apparently a renowned physician of Thessaly.

Text: Dr. Joseph Klar
Stamp: Minkus Publications, Inc., New York

Continued from page 7

Although constitutional delay in development is recognized less frequently in girls than boys, this may be due to more ready cultural acceptance of the immature girl. In such girls therapy is usually withheld, although at times the administration of estrogens may be warranted.

What is the acceptable treatment today of true sexual precocity, and what can be expected with the treatment?

There is no satisfactory treatment for idiopathic true, complete sexual precocity. Boys with sexual precocity should be evaluated periodically with neurologic and ophthalmologic examinations and skull roentgenograms to be certain not to overlook an intracranial neoplasm not manifest originally. If no underlying cause of the sexual precocity is found the parents should be reassured.

The patient should be dressed in loose fitting clothes, and every precaution must be taken to protect the child from unscrupulous individuals. Medroxyprogesterone (MPA) has been employed to treat children with sexual precocity. In girls MPA may interrupt menses and cause regression of the breasts.

However, this drug has no effect upon rapidly advancing skeletal maturation and has many side effects including aberrations of adrenal function, weight gain and fluid retention, alteration of chromosome morphology and prolonged suppression of the hypothalamic-pituitary axis.

It is not approved by the Food and Drug Administration for this purpose. In selected patients its use may be justified, however. Eventually, children with sexual precocity become less obvious as their peers achieve sexual maturation. However, children with sexual precocity become short adults as there is premature fusion of the epiphyses.

We know Librium works.
(chlordiazepoxide HCl)

We're still learning more about how and why.

Value of continuing animal research

Clinical knowledge of Librium is extensive, yet its mode of action remains under continuing study. Data from animal experiments have been presented here for their intrinsic interest and because such findings often provide direction to new research, both experimental and clinical. *However, conclusions from such studies may not always be extrapolated to humans.*

Is the limbic system the "Librium (chlordiazepoxide HCl) system"?

A great deal of experimentation on various animal species suggests that the limbic system is the principal site of action of Librium. Thus, in freely moving cats with electrodes implanted in the brain, Librium 5 mg/kg i.p. slowed electrical activity in the hippocampus, amygdala and septal areas but not in the neocortex which was significantly affected only at higher doses.[1,2] Current investigations on monkeys,[3,4] however, indicate that other subcortical structures may be implicated in the effect of Librium.

Other investigators, through electrophysiologic studies[5] in intact, conscious cats and monkeys, have demonstrated that chlordiazepoxide activates structures involved in the rewarding system—the preoptic area, lateral hypothalamus, septal region and hippocampal formation. At the same time, it appears to *inhibit* structures implicated in aversive behavior—the thalamic nuclei of the diencephalon and the midbrain reticular formation (MRF).

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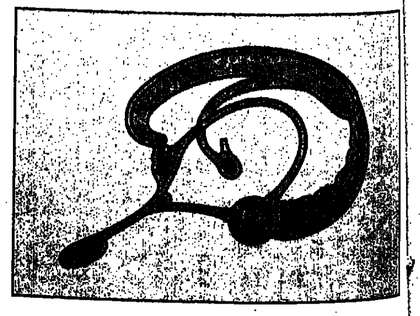

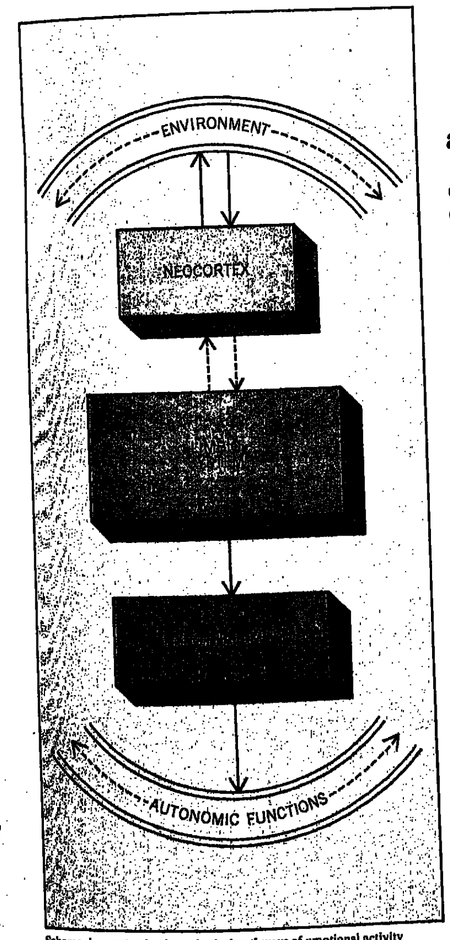

Schema demonstrating hypothetical pathways of emotional activity and its related expression in laboratory animals.

Clinical significance of excessive anxiety

Anxiety, when inappropriate and immoderate, may not only have adverse psychologic effects but may also cause various somatic disturbances. Reduction of excessive anxiety thus contributes to relief of anxiety-linked emotional and physical disorders.

Antianxiety action of Librium (chlordiazepoxide HCl)

The dependable action of Librium has been demonstrated in the relief of excessive anxiety and tension occurring alone or in association with functional and organic disorders—usually without adversely affecting performance. Librium is often used concomitantly, when anxiety is a contributing or complicating factor, with certain specific medications of other classes of drugs, *e.g.*, cardiac glycosides, diuretics and antihypertensives.

Adjunctive use of Librium is recommended when counseling, reassurance or other nonpharmacologic measures alone are not considered sufficiently effective. When anxiety has been reduced to manageable levels, therapy with Librium should be discontinued.

Librium®
(chlordiazepoxide HCl)
5 mg, 10 mg, 25 mg capsules

ROCHE

We're still learning more about it to make it more useful to you.

Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.
Contraindications: Patients with known hypersensitivity to the drug.
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.
Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.
Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

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Antiabortion Swing Worries Swiss, German, Italian MDs

Continued from page 1

Commenting on the case to MEDICAL TRIBUNE, a leading Swiss gynecologist noted that it took place in an area—Neuchâtel—that has hitherto been considered liberal in its interpretation of the existing legislation.

"As matters now stand, the law is applied in different ways in different cantons," Prof. William Geisendorf, of the University of Geneva, said. "Here in Geneva, for example, we take as our fundamental criterion the well-being of the mother, and so in practice we are close to the present situation in Britain and France."

Dr. Geisendorf, who recently visited the United States to study problems of family planning and abortion there, said the Neuchâtel decision seems to point to a stiffening of the conservative opposition to freer abortion, as in the United States.

The atmosphere in Italy is even more strained than in Switzerland or West Germany, following a police raid on an abortion clinic that was openly set up in Florence and provided operations by qualified medical staff at a fee of less than $100. Those now in prison awaiting trial include the gynecologist in charge of the clinic, Dr. Giorgio Conciani, and several of the nursing staff, and also Gianfranco Spadaccia, national leader of the Radical party, which established the clinic.

As the law—an inheritance from the Mussolini regime—now stands in Italy, anyone involved in an abortion faces a prison sentence of up to five years, and there are no extenuating circumstances.

In a recent decision, the Italian constitutional court ruled that abortions are legal whenever doctors determine that pregnancy is a serious threat to the physical or psychological health of the mother, but the judges added that it is up to the Italian parliament to draw up more specific criteria.

Court Bars Liberalization

Medical Tribune World Service

BONN, W. GERMANY—A decision by the West German Constitutional Court in Karlsruhe to reject the proposed law liberalizing abortion has been greeted with approval by the German Medical Association (Hartmannbund) here.

The law, which was accepted by a parliamentary majority last spring, was found unconstitutional by the Karlsruhe judges on the ground that it would violate the fetus's right to life.

Under the proposed law, physicians would have been permitted to carry out abortions up to the end of the 12th week of pregnancy, in line with legislation now in force in Great Britain, France, and the Scandinavian countries.

Interim Guidelines

A new law must now be drafted by the German Government, but the court noted that in the interim period it would be permissible for a physician to carry out an abortion on one of three grounds:

- *Ethical*—e.g., if the mother was pregnant as a result of rape.
- *Genetic*—if there is a danger of fetal malformation.
- *The Health of the mother*, mental or physical, if it could be endangered by the pregnancy.

A spokesman for the German Medical Association, a voluntary body that includes some 30,000 of the nation's 115,000 practitioners of medicine, said they welcomed the Court's decision because it upholds the fetus's right of protection.

"We also welcome the Court's position on permissible types of abortion because the emphasis is placed on medical rather than social considerations," the official told MEDICAL TRIBUNE.

"In our view the fetus becomes viable at nidation—or about a fortnight after conception and acquires individual rights that must be respected."

Fetal Viability Floor Placed at 22 Weeks

Medical Tribune World Service

GENEVA—An infant born before 22 weeks of gestation (under 500 G.) has no possibility of survival in the present state of medical knowledge, a World Health Organization scientific group has decided.

The W.H.O. experts, including Dr. Helen M. Wallace, Professor and chairman, Maternal and Child Health, School of Public Health, University of California, Berkeley, and Swiss gynecologist Prof. Hubert de Watteville of Geneva, Cantonal Hospital and University Clinic, came to the conclusion that infants delivered between 22 and 28 weeks (500 to 999 G.) have a "survival potential," but noted that such potential is extremely limited.

Less than 10% Survival

Available statistics show that fewer than 10 per cent of such infants survive, even in the most advanced centers.

"After 28 weeks' gestation (1000 G.) the fetus can be considered to have reached a stage of development where, if delivered alive, it has a reasonable expectation of survival," the group said in a WHO report.

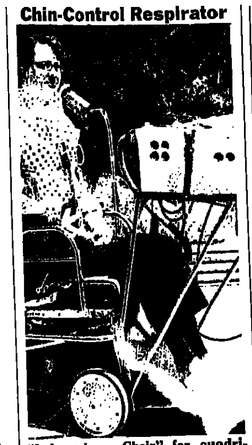
The experts, who also included scientists, physicians, and public health specialists from Britain, France, U.S.S.R. Israel, and Jamaica, have thus moved the limits for viability of the fetus further into the period of gestation than a British group who studied the question in 1972 and recommended that a period of 20 weeks or a weight of 400-500 G. should be considered as the criterion.

Austrian Doctor Boycott

Medical Tribune World Service

VIENNA—More than 80 per cent of Austrian gynecologists have announced that they will boycott for professional considerations new legislation permitting abortion within the first three months of pregnancy. As a result, only 12 of the country's 83 main hospitals are accepting women seeking such intervention.

Chin-Control Respirator



"Independence Chair" for quadriplegics susceptible to respiratory distress is equipped with portable respirator activated by chin-controlled drive unit.

Hastings Favors Deliberation on Malpractice Bill

Continued from page 3

Now, in contrast, the congressman is hearing from almost everyone about the malpractice insurance problem. "Doctors more than anybody, of course; other professions too, but primarily the doctors," Mr. Hastings said. They're mainly concerned about 'Am I covered or not?'"

"Strangely enough, the person who has not expressed his concern is the person who really should, and that is the prospective patient. I don't hear from the average on-the-street constituent on this problem very often, although when you realize that malpractice insurance increases have added $3 or $4 a day to hospital rates you would think that the average person would be worried about the high cost of health care. I presume that most people feel they're covered by some form of insurance and so aren't really concerned about the high cost."

Hastings Plans Bill

The medical malpractice insurance conference which Mr. Hastings and the AGPA sponsored included as participants a wide variety of persons concerned with the problem—Sen. Edward M. Kennedy (D.-Mass.) and Rep. Paul G. Rogers (D.-Fla.), chairmen of the Senate and House health subcommittees, respectively, representatives of the insurance industry and bar associations, state legislators and insurance commissioners, Department of Health, Education, and Welfare officials, academicians, and spokesmen for the American Medical and Hospital Associations.

Mr. Hastings indicated that it was likely he would introduce a bill dealing with the malpractice insurance problem since, "I don't think we have a long, long time [for detailed study of every aspect] and are going to have to do something about it."

Tribune Economic Analysis

Fuel Cost Jump Deepens Crisis in Real Estate

By Elliott Janeway

Publishing Economist

Thanks to the sixfold increase in the cost of fueling the country's structures, the real estate crisis is deepening. Last year, before incomes began to fall, but after fuel costs had taken their ghastly jump, a disturbing cross section of American owners of income-producing property found themselves in deep trouble. They were unable to break even on just their operating costs. Interest delinquencies ruined the REITS (Real Estate Investment Trusts) and contributed to the squeeze on the banks.

The threat of still higher fuel costs is pushing the panic button in the mortgage market. Owners of first mortgages "want out" at any salvage price. Lending institutions are anxious to avoid the complications and embarrassments that have been accompanying property ownership. They are taking their losses on "fire sales" of their mortgages instead of foreclosing on them.

Corporate bond prices rated as "businessman's risks" follow the mortgage market. The deep discounts on mortgages are forcing sympathetic discounts on a wide range of corporate bonds with such ratings. Ironically, however, it was the headlined drop in prime interest rates that triggered the stock market's tremendous comeback. Confidence in still lower prime rates has been generating the momentum the market has developed.

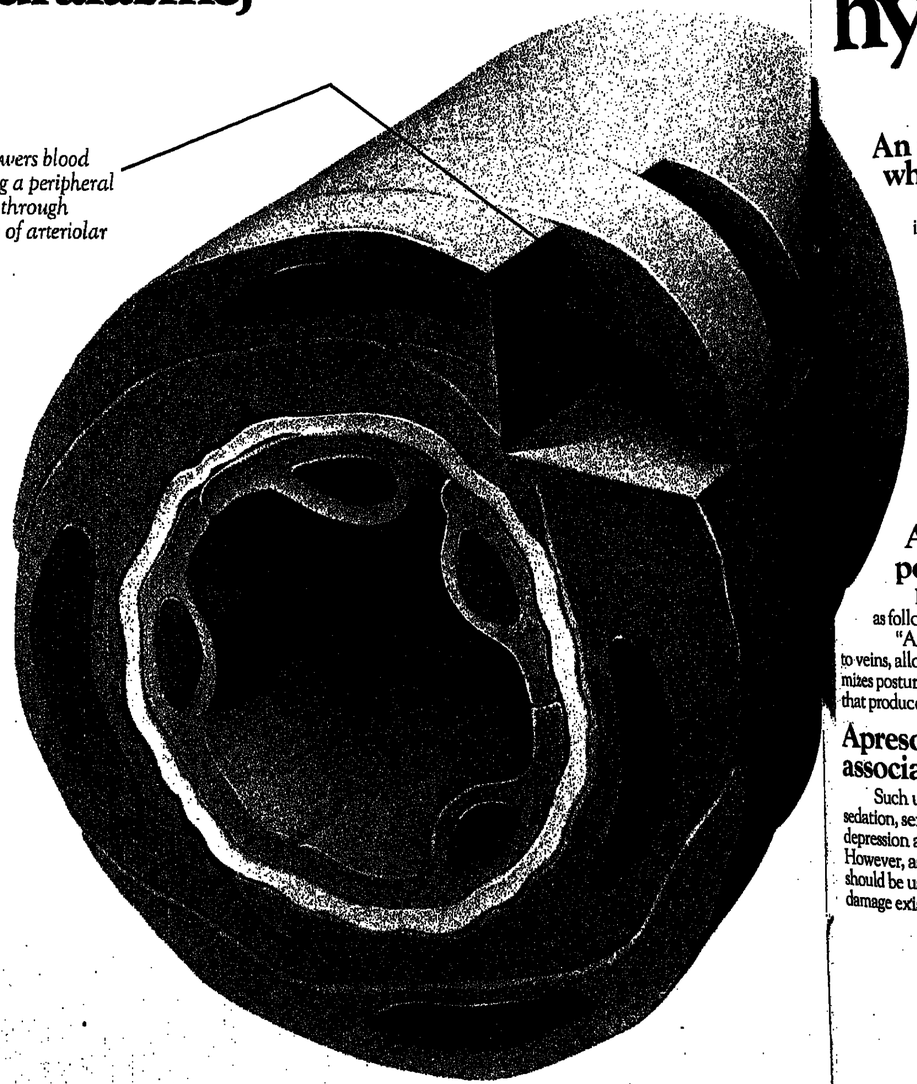
But the parameters of the American economy are by no means limited to prime rate borrowers. In fact, they can expect to remain in good shape only as long as they can count on collecting from their customers. The divergence between confidence in still lower prime rates and panic about even more real estate and entrepreneurial bankruptcies suggests that the stock market may have gotten considerably ahead of itself.

I own a good many shares in a mutual fund. Most of my friends have taken a beating in their mutual funds. How do you evaluate them at this time? I am now 60 years old, have a busy practice, calculate my net worth, which is real estate, at $500,000. Land which I purchased after World War II for $20,000 is now bringing me $15,000 annually and paying off a $100,000 mortgage on it. Would it be advisable to sell off the real estate in favor of Treasury bills?

Illinois specialist

The best mutual funds are the seasoned ones which have demonstrated a capacity to grow through bad markets. If you have owned yours for some time, yours may be one of the more conservative survivors. I see no reason for you to switch out of your position, although you might, in your position, consider one-year tax exempts. They may be obtained through any bank or broker.

Apresoline® (hydralazine)...where the action is in treating hypertension



Apresoline lowers blood pressure by exerting a peripheral vasodilating effect through a direct relaxation of arteriolar smooth muscle.

An antihypertensive idea whose time has come

Doctors who treat hypertension are increasingly interested in the one oral drug that has a mechanism of action exclusively its own—Apresoline.

Apresoline is in an antihypertensive class by itself because it reduces blood pressure through a unique mechanism. Acting at the ultimate site of hypertension, it directly relaxes arteriolar smooth muscle to decrease peripheral vascular resistance and arterial pressure. As blood pressure falls, there is an accompanying rise in cardiac output and rate.

Apresoline also maintains or increases renal and cerebral blood flow.

Apresoline minimizes postural hypotension

Nickerson[1] describes the action of Apresoline as follows:

"A preferential effect on arterioles, as compared to veins, allows the increase in cardiac output and minimizes postural hypotension; the latter is much less than that produced by agents blocking sympathetic nerves."

Apresoline avoids side effects associated with other agents

Such untoward reactions as drowsiness, lethargy, sedation, sexual dysfunction, and exacerbation of mental depression are not usually encountered with Apresoline. However, as with any antihypertensive agent, hydralazine should be used with caution where advanced renal damage exists.

Apresoline helps tailor the regimen to the patient

When Apresoline is added to an existing antihypertensive regimen, it introduces a different and complementary pharmacologic approach to the control of your patient's hypertension.

Apresoline thus affords the physician a variety of combinations with which he can construct regimens more closely molded to individual requirements. According to Freis[2] such a combination of drugs, each with a different antihypertensive mechanism, is the most effective way to control blood pressure. This may also permit lower drug dosages.

Apresoline lends itself admirably to the contemporary antihypertensive rationale and its therapeutic goals: more vigorous and more effective control of blood pressure through a plurality of mechanisms.

Apresoline: used effectively in the VA studies

Apresoline was one of the three basic drugs used in two published VA cooperative studies.[3,4]

References: 1. Nickerson M: Antihypertensive agents and the drug therapy of hypertension, In Goodman LS, Gilman A (eds): *The Pharmacological Basis of Therapeutics*, ed 4, New York, The Macmillan Company, 1970, p 729. 2. Freis ED: Hypertension: a controllable disease. *Clin Pharmacol Ther* 13:627-632, 1972. 3. Effects of treatment on morbidity in hypertension: Results in patients with diastolic blood pressures averaging 115 through 129 mm Hg, Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 202:1028-1034, 1967. 4. Effects of treatment on morbidity in hypertension: II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg, Veterans Administration Cooperative Study Group on Antihypertensive Agents. *JAMA* 213:1143-1152, 1970.

Next page: Apresoline (hydralazine) and the Hypertension Task Force

Apresoline® hydrochloride (hydralazine hydrochloride)

TABLETS

INDICATIONS
Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS
Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.

WARNINGS
Chronic administration of doses over 400 mg per day may produce an arthritis-like syndrome leading to a clinical picture simulating acute systemic lupus erythematosus. This may also occur at lower doses. Most of these reactions are reversible upon withdrawal of therapy, but long-term treatment with steroids may be necessary and relapse have been detected many years later. Complete blood counts, L.E. cell preparations and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy, even though patient is asymptomatic. These studies are also indicated in the presence of any unexplained symptoms.
Use MAO inhibitors with caution.

Usage in Pregnancy
The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.

ADVERSE REACTIONS
Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; anginal syndrome. *Less frequent:* Nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; flushing; nasal congestion; dyspnea; paralytic ileus; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.

DOSAGE
Initiate therapy in gradually increasing dosages, adjust according to individual response. Start with 10 mg 4 times daily for the first 2 to 4 days, increase to 25 mg 4 times daily for balance of first week. For second and subsequent weeks, increase dosage to 50 mg 4 times daily. For maintenance, adjust dosage to lowest effective level.
The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of Apresoline.
In a few resistant patients, up to 200 mg Apresoline daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of Apresoline combined with a thiazide, reserpine, or both may be considered. However, when combining therapy, individual titration is essential to insure the lowest possible therapeutic dose of each drug.

HOW SUPPLIED
Tablets, 10 mg (pale yellow, dry-coated); bottles of 100 and 1000.
Tablets, 25 mg (pale blue, dry-coated); bottles of 100, 500, and 1000.
Tablets, 50 mg (lilac, dry-coated); bottles of 100, 500, and 1000.
Tablets, 100 mg (peach, dry-coated); bottles of 100.

Consult complete literature before prescribing.

CIBA Pharmaceutical Company
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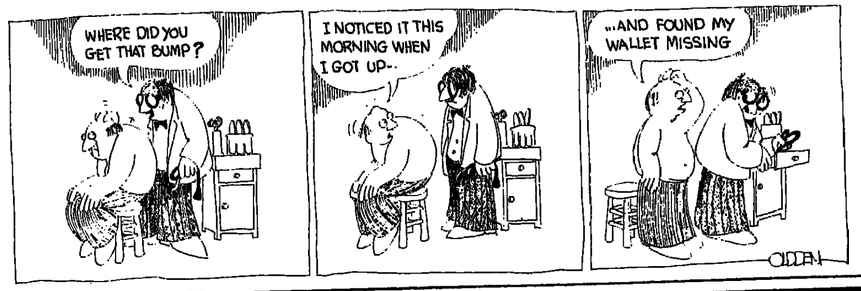
CIBA

Clinical Trials

by Oldden



TRIBUNE SPORTS REPORT

Data Lacking on What Effect 'The Pill' Has on Performance

Medical Tribune Report

CLEVELAND—Although many female athletes today are on oral contraceptives, there are no data on whether the medication benefits or hinders athletic performance or whether it may even present a health hazard in such patients, according to Dr. Lester Ballard, head of gynecology at the Cleveland Clinic.

"We need to find this out," he told a sports symposium there. "For the moment, however, all we can do is individualize and test each patient, to see if she is better on or off the pill. . . .

"Theoretically, a high-progestin pill could help athletic performance, but it's difficult to make a definitive statement about this potential because there hasn't been any study."

Such a pill, he noted, can also help the girl athlete with "heavy periods, breast tenderness, and bloating" due to hyperestrinism.

Slight Risk Seen

As to whether the use of oral contraceptives might make the female athlete more susceptible to a cerebrovascular accident or phlebitis, Dr. Ballard said:

"I think there may be a slight risk, but again there's no good hard data on this. I do know that when we do gynecological elective surgery today because there is increased clotting, it's a good idea to have the girls off the pill for two or three months."

Dr. Ballard was one of several speakers, including a woman coach, who addressed themselves to questions of female physiology and its relationship to participation in sports.

"Today, with all the dieting that's going on, many girls need supplemental iron," Dr. McLaughlin said. "Taking the blood counts of the girls on our teams—they were a bit low, and just on that basis I'd recommend iron for about 75 per cent of them . . . not because they're athletes, but just for their general health."

Does menstruation itself have any effect on sports performance? According to Dr. Ballard, it does for the girl who suffers cramps, headache, and fluid retention, and whose symptoms a birth-control pill does not help to alleviate. Some girls, however, fell better able to compete during their menstrual periods, he noted.

"The perineal pads should be thrown away" by athletes and by other girls as well, he said. For those with heavy periods, he recommended the use of two tampons instead of one.

With regard to swimming during menstruation, he commented:

"There's no problem because the vagina does exclude water. Also, the blood from the endometrium is sterile, and the only thing the blood picks up along the way is the normal vaginal flora, which is similar to what is found in the nasopharynx. So there's no problem if the blood does escape into the water of the pool."

Judy Devine, field hockey and basketball coach at Kent State University, Kent, Ohio, said that special breast protectors, such as plastic brassieres, do not seem warranted, even in the sports she coaches, with a fairly high degree of body contact.

"I have not found any incidence of breast contusion that amounts to anything at all," she reported.

She added that she has no rule on whether a girl may compete bra-less.

"I do have a couple of girls who compete bra-less, but one always wears a swimsuit under her uniform. It is uncomfortable to run without some kind of support, and I think they know this, so they either wear a bra or they buy a tight blouse."

'Thermostat' Set Higher

Dr. Thomas McLaughlin, team physician for women's sports at Case Western Reserve University, said that besides the obvious differences in size, strength, and body fat between males and females, there is also the temperature-regulation mechanism to consider. Since the hypothalamic "thermostat" is set higher in females, they would be at higher risk of heat stroke and heat exhaustion in any kind of mid-August practice in heavy protective clothing, such as male football players endure, he said.

IMMATERIA MEDICA

Zero Mostel's Baggy Union Suit

We compulsively clip anything that amuses, outrages, fascinates, or reminds us of something. A hopeless ense, we'll admit; the missing Gollyer brother, my good wife says. And the sequelae are dreadful. You have to sit down and go through all these fantastic clips and throw them all out to make room for more.

We try to stay just about a year behind our blade. Thus it happened recently that we were again chortling happily over pictures of Zero Mostel running around in his union suit—long baggy underwear, to the denim generation—in the *New York Times* of Feb. 10, 1974. It's been a long time since we saw a union suit so well modelled. It reminded us of our father's, but it also reminded us of a story Zero once told.

He had been, he confided, going to see a psychiatrist about his inner man and had been having a terrible time. It seemed that the psychiatrist considered him and his inner man very, very funny. He laughed uproariously at every story Zero told of his life in the spotlight, his pretzelless childhood, his adolescent struggles to become Babe Ruth and Rudolph Valentino, his poverty-ridden cold water flat and his efforts to be an abstract artist on the W.P.A.

Zero had the psychiatrist in the aisles, he told us with delight. "And I am also paying him; which is a real tale of woe. When is treatment going to begin? Am I always going to be onstage?" he howled.

The psychiatrist had his office couch within one of his apartment's large rooms. One day as Zero was detailing his hilarious misery, the psychiatrist was laughing so hard that tears were running down his cheeks. As Zero's story began to mount, the psychiatrist cried out, "Stop! Stop!"

Ah, thought Zero, treatment is at last to begin. He quieted instantly.

The psychiatrist, wiping away his tears, bounded for the door. "Do you mind if I bring in my wife?"

It was a wonderful treatment, Zero said. It cured him and his inner man. What a psychiatrist!